

In patients with pulmonary arterial hypertension (PAH, WHO Group I)

Using **REVEAL 2.0** and **REVEAL Lite 2** for regular risk assessment

Digital Risk Assessment Form

PAH is a progressive disease, even for mildly symptomatic patients

Patients with PAH Can Be at Greater Risk Than They Appear: Findings From the REVEAL Registry*



- **Almost 1 in 4 (24%, 58/244) of PAH-related hospitalizations occurred in newly diagnosed FC II patients^{1†}**
- **More than half of PAH-related hospitalizations (56%, 136/244) occurred in newly diagnosed FC III patients^{1†}**

Gestalt Assessment May Underestimate Patient Risk



In a survey, 41% (50/121) of treatment decision-makers reported not using a formal tool to assess risk in patients with PAH^{2‡}

- **90% of these decision-makers** reported that they relied on gestalt



A retrospective chart analysis of **patients considered low risk by gestalt** showed that^{3§}:

- **11% to 36% were categorized as intermediate risk** using various formal risk assessment tools (n=63 and 47, respectively)
- **4% to 28% were categorized as high risk** using various formal risk assessment tools (n=46 and 47, respectively)

*REVEAL (Registry to Evaluate Early and Long-term PAH Disease Management) was a US-based, observational registry involving 55 academic and community-based treatment centers. 3515 patients enrolled between March 2006 and December 2009. REVEAL was funded and sponsored by Actelion Pharmaceuticals US, Inc.⁴

[†]Newly diagnosed defined as within 90 days of registry enrollment. Analysis evaluated 862 newly diagnosed patients for first-time hospitalization. Hospitalizations were categorized as PAH related or PAH unrelated based on case report forms. Categories were defined prior to independent review. Of the 862 patients, 257 were hospitalized for PAH, of which 244 patients had available FC assessment. Data shown represent patients with a PAH-related hospitalization and FC assessment.

[‡]One hundred twenty-one PAH treatment decision-makers (physicians, nurse practitioners, and physician assistants) in the US were surveyed between February 7 and March 10, 2019 on their utilization of formal risk assessment tools in PAH management in clinical practice settings. Respondents could report using only clinical gestalt for risk assessment or choose from a number of formal risk assessment tools, including the REVEAL risk calculator, the French Pulmonary Hypertension Registry (FPHR) risk scoring system, the European Society of Cardiology (ESC)/European Respiratory Society (ERS) Guidelines for risk assessment, Comparative Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension (COMPERA) risk stratification, the Swedish Pulmonary Arterial Hypertension Registry (SPAHR) risk assessment, or another tool (unspecified). Medical writing support was funded and sponsored by Actelion Pharmaceuticals Ltd.

[§]Medical charts of 153 patients with FC II PAH were retrospectively analyzed to compare the results of risk assessment by clinical gestalt to those using formal risk assessment tools. COMPERA risk assessment classified 11% (n=63) of patients considered low risk by gestalt as intermediate risk. Using modified noninvasive FPHR, 36% (n=47) of patients considered low risk by gestalt were categorized as intermediate risk and 28% (n=47) as high risk. REVEAL 2.0 risk assessment classified 20% (n=46) of patients considered low risk by gestalt as intermediate risk and 4% (n=46) as high risk.

Guideline recommendations support regular risk assessments to help guide PAH treatment decisions



Achieving low-risk status is the goal of PAH treatment^{5,6}

- Usually associated with improved outcomes^{7,8}
- Consider treatment escalation in patients not achieving low-risk status
- Conduct follow-up risk assessment every 3 to 6 months



Simplified REVEAL Lite 2 complements REVEAL 2.0 in clinical practice^{7,8}

REVEAL 2.0: Refinement of the original REVEAL risk calculator

13 PARAMETERS

- **Treatment-naïve patients:**
Recommended to be used at baseline, 4- to 6-month, and yearly evaluations
- **Established patients:**
Recommended to be used at yearly evaluation

REVEAL Lite 2: Simplified method with similar risk discrimination to REVEAL 2.0

6 PARAMETERS

- Recommended to be used in both treatment-naïve and established patients
- Recommended to be used in routine clinical practice between full REVEAL 2.0 assessment to monitor trajectory

Please find an example of how this tool can be used below.

Note: The patient information contained in this example is not from a real patient. It is solely intended to demonstrate how to use the tool.

| DATE OF CHECKUP: 12/01/2020 | | REVEAL Lite 2 | | REVEAL 2.0 | |
|--|--|--|---------------------|--------------------|---------------------|
| PROGNOSTIC PARAMETERS | | SCORING | | PATIENT ASSESSMENT | |
| Renal insufficiency | eGFR <60 mL/min/1.73 m ² , or defined by clinical judgment if eGFR is not available (+1) | eGFR ≥60 mL/min/1.73 m ² , or defined by clinical judgment if eGFR is not available (0) | +1 | | +1 |
| NYHA or WHO FC | FC I (-1) FC II (0) FC III (+1) FC IV (+2) | | 0 | | 0 |
| Vital signs | Systolic blood pressure <110 mmHg (+1) Systolic blood pressure ≥110 mmHg (0) | | +1 | | +1 |
| | Heart rate >96 beats/min (+1) Heart rate ≤96 beats/min (0) | | +1 | | +1 |
| 6MWD | ≥440 m (-2) 320 m to <440 m (-1) 165 m to <320 m (0) <165 m (+1) | | -1 | | -1 |
| BNP/NT-proBNP | BNP <50 pg/mL or NT-proBNP <300 pg/mL (-2) BNP 50 pg/mL to <200 pg/mL or NT-proBNP 300 pg/mL to <1100 pg/mL (0) BNP 200 pg/mL to <800 pg/mL (+1) BNP ≥800 pg/mL or NT-proBNP ≥1100 pg/mL (+2) | | -2 | | -2 |
| Etiology | PAH-CTD (+1) Heritable PAH (+2) PoPH (+3) All other etiologies (0) | | — | | 0 |
| Demographics | Males >60 years of age (+2) Females and males ≤60 years of age (0) | | — | | 0 |
| All-cause hospitalization in last 6 months | Yes (+1) No (0) | | — | | 0 |
| Echocardiogram | Pericardial effusion (+1) No pericardial effusion (0) | | — | | +1 |
| PFT | % predicted DLco <40% (+1) % predicted DLco ≥40% (0) | | — | | 0 |
| RHC within 1 year | mRAP >20 mmHg (+1) mRAP ≤20 mmHg (0) PVR <5 Wood units (-1) PVR ≥5 Wood units (0) | | — | | 0 |
| | | | +6 | | +6 |
| | | | TOTAL | | |
| | | | 6 | | 7 |
| | | | (intermediate risk) | | (intermediate risk) |

6MWD=6-minute walk distance; BNP=brain natriuretic peptide; DLco=diffusing capacity of the lungs for carbon monoxide; eGFR=estimated glomerular filtration rate; FC=functional class; mRAP=mean right atrial pressure; NT-proBNP=N-terminal pro-brain natriuretic peptide; NYHA=New York Heart Association; PAH=pulmonary arterial hypertension; PAH-CTD=PAH associated with connective tissue disease; PFT=pulmonary function tests; PoPH=portopulmonary hypertension; PVR=pulmonary vascular resistance; RHC=right heart catheterization; WHO=World Health Organization.

LOW RISK: 1 TO 5

INTERMEDIATE RISK: 6 TO 7

HIGH RISK: ≥8

LOW RISK: 0 TO 6

INTERMEDIATE RISK: 7 TO 8

HIGH RISK: ≥9

Use the REVEAL 2.0 and REVEAL Lite 2 risk score calculators below to assess your patients and track their risk factors. Fill in response for each determinant.

DATE OF CHECKUP: _____

REVEAL Lite 2

REVEAL 2.0

| PROGNOSTIC PARAMETERS | SCORING | PATIENT ASSESSMENT | |
|--|--|--------------------|----|
| Renal insufficiency | eGFR <60 mL/min/1.73 m², or defined by clinical judgment if eGFR is not available (+1) eGFR ≥60 mL/min/1.73 m², or defined by clinical judgment if eGFR is not available (0) | | |
| NYHA or WHO FC | FC I (-1) FC II (0) FC III (+1) FC IV (+2) | | |
| Vital signs | Systolic blood pressure <110 mmHg (+1) Systolic blood pressure ≥110 mmHg (0) Heart rate >96 beats/min (+1) Heart rate ≤96 beats/min (0) | | |
| 6MWD | ≥440 m (-2) 320 m to <440 m (-1) 165 m to <320 m (0) <165 m (+1) | | |
| BNP/NT-proBNP | BNP <50 pg/mL or NT-proBNP <300 pg/mL (-2) BNP 50 pg/mL to <200 pg/mL or NT-proBNP 300 pg/mL to <1100 pg/mL (0) BNP 200 pg/mL to <800 pg/mL (+1) BNP ≥800 pg/mL or NT-proBNP ≥1100 pg/mL (+2) | | |
| Etiology | PAH-CTD (+1) Heritable PAH (+2) PoPH (+3) All other etiologies (0) | — | |
| Demographics | Males >60 years of age (+2) Females and males ≤60 years of age (0) | — | |
| All-cause hospitalization in last 6 months | Yes (+1) No (0) | — | |
| Echocardiogram | Pericardial effusion (+1) No pericardial effusion (0) | — | |
| PFT | % predicted DLCO <40% (+1) % predicted DLCO ≥40% (0) | — | |
| RHC within 1 year | mRAP >20 mmHg (+1) mRAP ≤20 mmHg (0) PVR <5 Wood units (-1) PVR ≥5 Wood units (0) | — | |
| | | +6 | +6 |
| | | TOTAL | |

Clear Form

LOW RISK: 1 TO 5

INTERMEDIATE RISK: 6 TO 7

HIGH RISK: ≥8

LOW RISK: 0 TO 6

INTERMEDIATE RISK: 7 TO 8

HIGH RISK: ≥9

References: 1. Burger CD, Long PK, Shah MR, et al. Characterization of first-time hospitalizations in patients with newly diagnosed pulmonary arterial hypertension in the REVEAL Registry. *CHEST*. 2014;146(5):1263-1273. 2. Wilson M, Keeley J, Kingman M, Wang J, Rogers F. Current clinical utilization of risk assessment tools in pulmonary arterial hypertension: a descriptive survey of facilitation strategies, patterns, and barriers to use in the United States. *Pulm Circ*. 2020;10(3):2045894020950186 and suppl. doi:10.1177/2045894020950186 3. Sahay S, Tonelli AR, Selej M, Watson Z, Benza RL. Risk assessment in patients with functional class II pulmonary arterial hypertension: comparison of physician gestalt with ESC/ERS and the REVEAL 2.0 risk score. *PLoS One*. 2020;15(11):e0241504. doi:10.1371/journal.pone.0241504 4. McGoon MD, Miller DP. REVEAL: a contemporary US pulmonary arterial hypertension registry. *Eur Respir Rev*. 2012;21(123):8-18. 5. Galiè N, Humbert M, Vachiéry JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J*. 2015;46(4):903-975. 6. Galiè N, Channick RN, Frantz RP, et al. Risk stratification and medical therapy of pulmonary arterial hypertension. *Eur Respir J*. 2019;53(1):1801889. doi:10.1183/13993003.01889-2018 7. Benza RL, Gomberg-Maitland M, Elliott CG, et al. Predicting survival in patients with pulmonary arterial hypertension: the REVEAL risk score calculator 2.0 and comparison with ESC/ERS-based risk assessment strategies. *CHEST*. 2019;156(2):323-337. 8. Benza RL, Kanwar MK, Raina A, et al. Development and validation of an abridged version of the REVEAL 2.0 Risk Score Calculator, REVEAL Lite 2, for use in patients with pulmonary arterial hypertension. *CHEST*. 2020;S0012-3692(20):34296-3. doi:10.1016/j.chest.2020.08.2069



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